ORIGINAL ARTICLE

ASSESSING NUTRITIONAL STATUS OF CRITICALLY ILL PATIENTS USING SERUM PREALBUMIN LEVELS

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Background: Malnutrition in hospitalized patients, contributes to poor outcomes. Biomarker serum prealbumin, can prevent the complications by commencement of nutritional support to improve clinical outcomes. This study was designed to assess the association between low serum prealbumin level (<18 mg/dl), with length of stay and all cause intensive care unit mortality. **Methods:** This cross-sectional study was conducted from July 2016 to July 2017 at Aga Khan University Hospital Karachi Pakistan. All consecutive patients, aged between 18 to 70 years, admitted in medical or surgical intensive care unit were included. Demographic, clinical history and blood samples for analysing serum prealbumin were obtained on first day of admission. Patients were categorized into two groups based on their serum prealbumin level (taking <18 mg/dl as low). **Results:** A total of 139 patients were included in this study; 95 (68.3%) were male. Median (Q3-Q1) prealbumin level of 12.3 mg/dl (18.8–8.7) was observed with low prealbumin level (<18 mg/dl) in 100 (71.9%) patients. All-cause mortality was observed in 26 (26.0%) patients, mortality rate was significantly higher in patients with low prealbumin level (26.0% vs. 17.9%), *p*-value =0.31). Hospital and intensive care unit length of stay were statistically insignificantly different between the two groups with *p*-values of 0.27 and 0.44 respectively. **Conclusion:** We did not find association of low serum prealbumin with length of stay and mortality. Further research is warranted for the assessment of prealbumin as independent predictor of ICU mortality.

Keywords: Prealbumin; Length of stay; Mortality; Intensive care unit

Citation: Arbab K, Majid H, Jafri L, Akram B, Raheem A, Jamil B, *et al*. Assessing Nutritional Status of Critically Ill Patients Using Serum Prealbumin Levels: A Single Centre Cross-Sectional Study. J Ayub Med Coll Abbottabad 2019;31(2):178–81.

INTRODUCTION

According to American Society of Parenteral and Enteral Nutrition, malnourishment is defined as "an acute, subacute or chronic state of nutrition, in which a combination of varying degrees of overnutrition or undernutrition with or without inflammatory activity led to a change in body composition and diminished function".[1] An estimated 2 billion world population is malnourished, which is increasing globally but especially in developing countries.[2]

Poor nutritional status contributes to poor outcomes like; prolonged length of stay (LOS) in hospital, increased readmission rates, occurrence of disease complications. This in turn leads to increased overall cost of care and all-cause mortality. Incidence of malnutrition in hospitalized patients is estimated to be as high as 40–50% of all hospitalized patients.[3] If identified early, malnourishment in hospitalized patients can be prevented by early commencement of nutritional support leading to improvement in clinical outcomes and reduction in overall cost.

There are different methods used to classify malnutrition ranging from clinical signs and symptoms to anthropometric measures and biochemical tests. Despite all the advancements in field of healthcare, there is variability in malnourishment assessment techniques and it is dependent on expertise of personnel assessing the nutritional status. Serum albumin is a widely used indicator of the status of nutrition[4] but due to its long half-life of 3–4 weeks; acute changes in nutritional status cannot be determined. There is a need to identify accurate, rapid and sensitive biomarkers for nutritional assessment.

Prealbumin also known as transthyretin provides a recent index of nutritional status. However, its predictive value in assessing nutritional status of critically ill patients is not well studied. Thus, this study was designed to assess clinical utility of prealbumin in identifying the nutritional status in critically ill patients and evaluate its association with LOS in hospital and all-cause mortality.

MATERIAL AND METHODS

This cross-sectional study was conducted at Departments of Pathology and Laboratory Medicine, Medicine and Anaesthesiology of Aga Khan University Hospital Karachi Pakistan. Approval of institutional ethical review committee was taken before commencement of the study (ERC ID: 3930-Pat-ERC-

15). Patient admitted to intensive care unit (ICU) within 12 hours of admission from July 2016 to July 2017 were invited to participate in the study after informed consent from the legal care taker or guardian. Patients with history of chronic liver disease, on dialysis, with history of alcohol, and prednisolone intake and diagnosed nephrotic syndrome were excluded. Also, the patients admitted to wards and then shifted to ICU due to deterioration of underlying condition were excluded to decrease effect of prolong hospital admission. Patients were included before initiation of any nutritional support. One hundred and thirty-nine patients were finally analysed and followed up till the patients were discharged from ICU or after shifted to ward, special care or expired during hospitalization.

Their demographic details such as gender, age, weight and height were recorded using structured questionnaire and BMI was calculated. Patient's last two months clinical history with regards to hospitalization, weight loss, history of vomiting, diarrhoea, anaemia, loss of appetite, and difficulty in chewing and swallowing was taken along with LOS in ICU, LOS in hospital and mortality status. Five millilitres of blood sample for prealbumin was collected in a gel tube and stored at -80^{o}C until analysis. All enrolled patients were observed during their hospital stay for ICU LOS, hospital LOS and all-cause mortality.

Serum prealbumin was analysed by nephelometric method on Image 800 Chemistry analyser (Beckman Coulter Inc. NY, US) using Beckman Coulter's serum prealbumin kit. For assessing system performance and validating results, three levels of manufacturer provided internal quality controls were run with each batch of prealbumin. Serum prealbumin cut-off of >18mg/dl was labelled as normal.

Collected data were entered and analysed using Statistical Package for the Social Sciences (SPSS version 21 and R version 3.4.3). Normality of distribution for continuous variables was assessed using Shapiro-Wilk test and appropriate median (Q3-Q1) was calculated. Categorical variables were expressed as frequency and percentage. Patients were categorized into two groups based on their prealbumin level (<18 mg/dl and ≥18 mg/dl). Association of low prealbumin level (<18 mg/dl) with categorical variables were examined using the Chi-square test. The association between continuous variables and low prealbumin level were examined using the Mann-Whitney test. A *p*-value of ≤0.05 was taken as criteria for statistical significance. Univariate and multivariate logistic regression was performed taking low prealbumin levels as independent variable. Two-sided *p*-value of ≤0.05 was taken as criteria for statistical significance.

RESULTS

A total of 139 patients were included in this study, of which 95 (68.3%) were male. Median age of the patients was 47 years (64–32) and median BMI was 26 kg/m² (29.4–24). Majority of the patients 58 (41.7%) were either overweight or obese. Median prealbumin level was 12.3 mg/dl (18.8–8.7). Low prealbumin level (<18 mg/dL) was seen in 100 (71.9%) patients. Fifty-two (37.4%) of patients, belonged to service of neurosurgery, followed by surgery 29 (20.9%), general medicine 54 (38.8%), and orthopaedics' 4 (2.9%). All cause ICU mortality was observed in n=33 (23.7%) of the study patients. Demographic and other characteristics of the patients are presented in table-1.

Comparison of association of clinical characteristics and study outcomes with low and optimal prealbumin are presented in table-2.

Significant association of low prealbumin level was observed with history of hospitalization and vomiting in past two months. All-cause mortality was observed in 33 (23.7%) patients; mortality rate was higher in patients with low prealbumin as compare to those with level more than 18mg/dl but it was not statistically significant {26 (26%) vs. 7 (17.9%) *p*-value = 0.31)}. Median hospital and ICU length of stay were different between the two groups (*p* value >0.05). Median prealbumin level was found to be significantly higher in survived patients, 13.9 mg/dl (19.1–10.3) vs. 9.7 mg/dl (16.8–6.8), as compared to patients who expired (*p*-value of 0.02).

After adjusting for all the potential factors in multivariate linear regression analysis, none of the factors were found to correlate with prealbumin. Table-3 depicts the univariate and multivariate analysis of low prealbumin blood level against different baseline characteristics.

Table-1: Demographic and clinical characteristics of the patients admitted to ICU (n=139)

Characteristics	Frequency (%) or Median (IQR)
Gender	
Male	95 (68.3%)
Female	44 (31.7%)
***Age** years	47(64-32)
Up to 50	73 (52.5%)
≥ 50	66 (47.5%)
***Body Mass Index (BMI)** kg/m^2	26.0(29.4-24.0)
Underweight [<18.5]	5 (3.6%)
Healthy [18.5 <23]	19 (13.7%)
Overweight [23- 27]	58 (41.7%)
Obese [BMI ≥ 27]	57 (41.0%)
***Prealbumin** mg/dl	12.3 (18.8-8.7)
<18	100 (71.9%)
≥18	39 (28.1%)
*Values are expressed as Median (IQR = Interquartile Range) as *hypothesis of the normality of the distribution was rejected with Shapiro-Wilk test *p*-value of <0.001	

Table-2: Comparison of clinical characteristic & study outcomes of patients admitted to ICU with low & optimal prealbumin levels (n=139)

	Frequency (%) n=139	Prealbumin Level		**p-value
		<18mg/dL n = 100	≥18mg/dL n = 39	
Past two months clinical history				
Past Hospitalization	31 (22.3%)	27 (27%)	4 (10.3%)	0.03*
Weight Loss	50 (36%)	38 (38%)	12 (30.8%)	0.42
Vomiting	34 (24.5%)	29 (29%)	5 (12.8%)	0.04*
diarrhoea (2–3 episodes\day)	16 (11.5%)	14 (14%)	2 (5.1%)	0.14
Loss of Appetite	44 (31.7%)	34 (34%)	10 (25.6%)	0.34
Difficulty in Chewing	9 (6.5%)	5 (5%)	4 (10.3%)	0.25
Difficulty in Swallowing	8 (5.8%)	7 (7%)	1 (2.6%)	0.31
Anaemia	38 (27.3%)	26 (26%)	12 (30.8%)	0.57
Study Outcomes				
LOS in Hospital (days) Median (IQR)	12 (18–8)	12 (18–8)	11 (16–7)	0.27
LOS in ICU (days) Median (IQR)	6 (9–3)	6 (10–3)	5 (7–4)	0.44
All cause ICU mortality	33 (23.7%)	26 (26.0%)	7 (17.9%)	0.31

*Statistically significant at 0.05 level of significance
**p-values are based on chi-square test for categorical variables and Mann-Whitney test for continuous variables
LOS = Length of stay
ICU = Intensive care unit
IQR = Interquartile Range

Table-3: Univariate and multivariate analysis of low prealbumin

Factors	Univariate Analysis		Multivariate Analysis	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Demographics				
Male	1.11 [0.51–2.45]	0.79	1.45 [0.6–3.49]	0.41
Age > 50 years	1.67 [0.78–3.54]	0.18	1.52 [0.66–3.48]	0.32
BMI ≥ 23 kg/m^2	0.83 [0.3–2.27]	0.71	1 [0.32–3.14]	0.99
Past two months clinical history				
Past Hospitalization	3.24 [1.05–9.97]	0.04*	2.82 [0.79–10.05]	0.11
Weight Loss	1.38 [0.63–3.04]	0.42	1.27 [0.46–3.5]	0.63
Vomiting	2.78 [0.99–7.81]	0.05	2.95 [0.95–9.15]	0.06
Diarrhoea	3.01 [0.65–13.92]	0.15	2.37 [0.43–13.24]	0.32
Loss of Appetite	1.49 [0.65–3.42]	0.34	0.73 [0.25–2.18]	0.57
Difficulty in Chewing	0.46 [0.12–1.81]	0.26	0.47 [0.1–2.25]	0.34
Difficulty in Swallowing	2.86 [0.34–4.04]	0.33	3.01 [0.32–28.61]	0.33
Anaemia	0.79 [0.35–1.78]	0.57	0.66 [0.26–1.65]	0.37
All cause ICU Mortality	1.61 [0.63–4.08]	0.31	1.56 [0.56–4.31]	0.39

Dependent variable = Low Prealbumin
OR=Odds Ratio, CI = Confidence interval
*Statistically significant at 5% level of significance

DISCUSSION

Since long serum albumin have been utilized by physicians for monitoring or evaluation of nutritional status. However, it has proved to be an ineffective measure for assessing recent changes in nutritional status, owing to its large plasma pool and long half-life of 3–4 weeks. On the other hand, prealbumin, has a half-life in plasma of 24–48 hours, which in comparison to albumin is much shorter. Hence it is relatively more responsive to alterations in energy-protein status in comparison to albumin and provides a better reflection of dietary intake that was recent rather than the overall status of the nutrition.[5] A raise in prealbumin can be expected within 4 days after nutritional support has been provided complemented with the intake of a high calorie/high protein formula.[6]

Malnourishment is a common finding in hospitalized patients and its early identification and correction is imperative for the better outcome of the patients. Low prealbumin is reported to be associated with higher in-hospital or short-term mortality and post procedural complication such as infection, extended hospital stays and mechanical support in patients with various underlying diseases.[7–11] This study was an attempt to assess the association between low prealbumin (<18 mg/dl), with LOS and all-cause mortality in our population.

In present study, 71.9% of the patients had low levels of prealbumin. Association of prealbumin was observed with past two month's history of hospitalization and vomiting. Lower prealbumin values in patients who expired as compared to those who survived were also noted. While LOS in ICU and hospital were longer in subjects with low

prealbumin (<18 mg/dl) levels; 6 days (10–3) and 12 days (18–8) compared to patients with optimal prealbumin 5 days (7–4) and 11days (16–7) respectively. However, none of the factors were significantly associated with serum prealbumin level in the regression model in this study.

Previous study by Cheng V *et al*[12] reported that low prealbumin was associated with critically ill trauma patients had high rate infections (p<0.001), more mortality (p-value 0.007), extended hospital stays (p<0.001), and longer ICU stay (p<0.001). Another study by Avram *et al*[13] documented that serum prealbumin was an independent forecaster of mortality in patients suffering from peritoneal dialysis. Similarly, another study by Yang HT *et al*[14] on massively-burned patients observed that serum prealbumin was independently associated with mortality. A study on critically ill patients by Devakonda A *et al*[15] found excellent concordance between protein energy malnutrition and serum prealbumin, additionally prealbumin levels correlated with mortality, ICU and hospital LOS. There are some limitations to our study; small sample size, single centre cross-sectional study design while serial monitoring may serve as a better predictor.

CONCLUSION

Low prealbumin concentration was common in critically ill patients. However, no association was found between low prealbumin and LOS or all-cause mortality in our population. For more generalizable results, future follow up, prospective and large, multicentre researches are needed.

AUTHORS CONTRIBUTION

KA: Got the funding, data collection, data entry and management, analysis and wrote initial manuscript. HM: Data management, Data analysis and wrote initial manuscript. LJ: Reviewed the manuscript for intellectual content. BA: patient recruitment, data collection, data entry, reviewed final manuscript. AR: Data analysis and reviewed final manuscript. BJ: facilitated data collection and patient recruitment, Reviewed manuscript for intellectual content. MH: developed study design, reviewed manuscript for intellectual content. AHK: Conceived idea, developed study design supervised research process and critically reviewed manuscript for intellectual content

Funding disclosure: The study was supported by Resident Research Grant from Department of Pathology & Laboratory Medicine, Aga Khan University.

Conflict of Interest: All authors have no conflict of interest to disclose.

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Submitted: 27 July, 2018	*Revised: 17 August, 2018*	*Accepted: 3 February, 2019*

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